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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (REV. 2/95)

1-File Copy

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Office Action Summary	Application No. 08/634,039	Applicant(s) Snider, Denis P.
	Examiner F. Pierre VanderVegt	Group Art Unit 1816

Responsive to communication(s) filed on _____ .

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-9* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) *1-9* is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

X See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948. SUBSTITUTE

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

X Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-9 are pending in this application.

1. The Petition to Correct Inventorship under 37 CFR 1.48(a) filed Nov. 22, 1996 and Consent of Assignee to Correction of Inventorship filed Jan. 20, 1997 have been received and duly noted. The intent of these papers is, however, unclear. Both documents authorize a change of inventorship to include only Denis P. Snider to the exclusion of Mark R. McDermott and Brian J. Underdown. The application currently lists Dr. Snider as the sole inventor, evidenced both by the file wrapper and the filing receipt. The original declaration submitted with the specification was not signed and the substitute declaration of Nov. 7, 1996 was signed only by Denis P. Snider. The names of Mark R. McDermott and Brian J. Underdown were lined through on the substitute declaration of Nov. 7, 1996. Therefore, Denis P. Snider is already listed as sole inventor and the proposed correction is not necessary.

It is further noted that on his declaration dated Nov. 5, 1996, that Brian J. Underdown, in item 2, does not consider himself to be an inventor of the claimed invention. On his declaration dated Nov. 5, 1996, Denis P. Snider, in item 2, claims to be sole inventor of the claimed invention. On his declaration dated Nov. 5, 1996, Mark R. McDermott, in item 2, also claims to be sole inventor of the claimed invention. This is in conflict with the said declaration of Denis P. Snider and also that of registered representative Michael I. Stewart dated Aug. 23, 1996.

Clarification and/or correction is required.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not state ~~whether~~ the inventor is a sole ~~or joint~~ inventor of the invention

claimed.

Claim Rejections - 35 USC § 112

3. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 5-7 are drawn to generating a protective immune response to a pathogen and the specification identifies an immune response by the ability to raise IgG and IgA antibodies specific for said antigen. It is noted that a substance which generates a protective immune response to a pathogen constitutes a vaccine. Roitt et al (W) teaches that to be effective a vaccine must induce a long-lived response from T cells which produce a long lived cell mediated immunity to the antigen and must not induce suppression (page 16.21, section entitled "VACCINES" in particular). Roitt et al further teaches that, although antigens are more easily identified by their interaction with immunoglobulins, immune protection is dependent upon the development of a good cell mediated immune response and thus antigens must be identified by their reactions with T cells to useful in vaccination (page 16.22, section entitled "STRATEGIES IN VACCINE DESIGN" in particular). Due to the lack of guidance provided in the specification, it would be unpredictable and require undue experimentation of a skilled artisan to determine which antigens would be able to generate a lasting T cell response based on the IgG or IgA response to the antigen. The state of the art does not allow one to predict T cell epitopes based on antigen reactivity with immunoglobulin molecules, as the immunogenic epitopes "seen" by these two separate arms of the immune response are often quite disparate.

Claims 1-9 are drawn to generating an immune response to an antigen in a host. Beyond the specific antigen exemplified in the specification, hen egg lysozyme, the specification does indicate how to determine peptides, proteins, carbohydrates or ligands which are capable of generating a competent immune response by the method claimed. The

specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in claims 1-9 without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides, proteins, carbohydrates or ligands broadly encompassed by the claims and the claims broadly encompasses a significant number of immunogens. Besides the specific antigen, hen egg lysozyme, disclosed in the specification, the specification fails to provide any guidance as to how to determine other suitable immunogenic proteins or epitopes. Since the amino acid or carbohydrate sequence of an antigen determines its structural, immunogenic and functional properties, predictability of which fragments would still retain functionality as a competent immunogen requires a detailed knowledge of the ways in which a protein's, carbohydrate's or ligand's structure relates to its binding characteristics and functional usefulness. However, the problem of predicting antigenic epitopes from a long list of pathogenic organisms, as in lines 2-29 of page 9 of the specification, from mere recitation of their names and exemplification using a single protein, hen egg lysozyme, and in turn utilizing fragments thereof is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the nature of the invention, quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al, U.S. Patent 4,950,480 (A), or Barber et al, U.S. Patent 5,194,254 (B), each in view of Wu et al (13).

The '480 patent teaches a method to confer protection against pathogenic organisms using monoclonal antibodies (mAbs) specific for membrane determinants expressed on mammalian antigen presenting cells as a targeting moiety which are coupled to antigens derived from pathogenic organisms (Abstract in particular). For example, a peptide from Herpes simplex virus was coupled to an anti-MHC class II mAb and elicited an IgG response (Example IV and Figure 4 in particular). The '480 patent further teaches that this method is helpful in the induction of antigen-specific IgG responses (Abstract in particular). The '254 patent provides the same teachings. The '480 patent and the '254 patent do not teach intranasal administration or a heterobifunctional linking molecule. Wu et al teaches the intranasal administration of *Streptococcus mutans* surface protein antigen I/II (AgI/II) coupled to cholera toxin B subunit (CTB)(Abstract in particular). AgI/II and CTB are coupled through a heterobifunctional linking molecule (page 315, subsection "Antigens" in particular). Wu et al also teaches that intranasal administration of the AgI/II-CTB complex induced IgG and IgA antibody production better than AgI/II alone (Figure 4 in particular) and required no further adjuvant for a strong salivary IgA response (page 320, first full paragraph in second column in particular) and that antibodies were found in response to the immunization in saliva as well as gut and tracheal washes (Table 1 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to be motivated to combine the teachings of the '480 or '254 patents concerning anti-APC mAb-antigen conjugates with the teachings of Wu et al concerning intranasal administration of antigen to elicit a protective response to pathogenic organisms. One would have been motivated, with a reasonable expectation of success to combine these teachings by the desire to elicit an antigen-specific,

rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms.

6. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al, U.S. Patent 4,950,480 (A), or Barber et al, U.S. Patent 5,194,254 (B), each in view of Wu et al (13) as applied to claims 1-6 and 8 above, and further in view of Dempsey et al (U) and ATCC Catalogue of Cell Lines and Hybridomas, Seventh Edition (V).

The '480 patent, '254 patent and Wu et al have been discussed supra. Wu et al further teaches that the nasal passages of rats and mice contain organized lymphoid tissue that is considered to be the equivalent of Waldeyer's ring in humans and that $CD4^+$ T cells (which are crucial in establishing an antigen-dependent immune response) outnumber $CD8^+$ T cells among intraepithelial and submucosal lymphocytes of nasal mucosae in humans (page 320, first paragraph of Discussion in particular). The combination of references does not teach a monoclonal antibody to human APCs. Dempsey et al teaches that conjugation of antigen to complement component C3d, which binds to CD21 on B cells, results in the production of antibodies to said antigen without addition of any additional adjuvants (see entire document, Figure 4 in particular). The ATCC catalogue offers for public sale the hybridoma which produces the anti-human C3d receptor (CD21) monoclonal antibody THB-5 (page 364, ATCC HB 135 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the THB-5 anti-human CD21 mAb for the anti-mouse mAb of the '480 or '254 patents and combine the teachings of the '480 patent concerning anti-APC mAb-antigen conjugates with the teachings of Wu et al concerning intranasal administration of antigen to elicit a protective response to pathogenic organisms. One would have been motivated, with a reasonable expectation of success to combine these teachings based on the teachings of Wu et al of similarities between the tissues of the nasal passages of humans and rodents and the high proportion of $CD4^+$ T cells in these tissues, the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is

often the first line of encounter of an immune system with pathogenic organisms and the ease of purification of a mAb from an established hybridoma cell line rather than isolation and purification of a complement component.

7. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al, U.S. Patent 4,950,480 (A), or Barber et al, U.S. Patent 5,194,254 (B), each in view of Wu et al (13), and Babington, U.S. Patent 4,228,795 (C).

The '480 patent, '254 patent and Wu et al have been discussed supra. The combination of references does not teach a disperser for dispersing an aerosol. The '795 patent teaches a nebulizer which can be used to aerosolize medicants for nasal inhalation (Figure 4 and column 6, line 7 through column 8, line 54 in particular). The '795 patent further teaches that said nebulizer is suitable for use with viscous or sticky substances (column 8, lines 34-37 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the nebulizer taught by the '795 patent to administer the mAb-pathogenic antigen conjugate taught by the combination of the '480 or '254 patents with Wu et al intranasally. One would have been motivated, with a reasonable expectation of success to combine these teachings by the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms and by the teachings of the '795 patent that the nebulizer is usable with sticky substances, which a common property of proteinaceous solutions.

Conclusion

8. Item # 46 on the Information Disclosure Statement (IDS) submitted Sep. 12, 1996 is lined through because it is a duplicate of item # 35 of the same IDS.

9. Papers related to this application may be submitted to group 1800 by facsimile transmission. Papers should be faxed to group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for Art Unit 1816 is (703)308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The examiner can normally be reached Monday through Friday from 8:00 am to 4:30 pm ET. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the group 1800 receptionist, whose telephone number is (703)308-0196.

February 3, 1997
F. Pierre VanderVegt, Ph.D.
Patent Examiner
Art Unit 1816

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP 1800